

Next step in antibiotic stewardship: Pharmacist-provided penicillin allergy testing

Z. Gugkaeva PharmD¹ | J. S. Crago PharmD Candidate, BS² | M. Yasnogorodsky PharmD Candidate³

¹Department of Pharmacy, Maury Regional Medical Center, Columbia, TN, USA

²College of Pharmacy, University of Tennessee, Nashville, TN, USA

³College of Pharmacy, Lipscomb University, Nashville, TN, USA

Correspondence

Z. Gugkaeva, Department of Pharmacy, Maury Regional Medical Center, Columbia, TN, USA.
Email: zgugkaeva@aol.com

Summary

What is known: Penicillin allergy limits therapeutic options for patients but often disappears over time, leaving patients erroneously labelled allergic and leading to the utilization of broad-spectrum and more expensive antibiotics. Penicillin allergy can be effectively assessed via skin testing.

Objective: To improve patient access to penicillin allergy testing by implementing a pharmacist-provided service in a hospital setting.

Comment: Beta-lactams remain a mainstream therapy for many infections due to their effectiveness, low side effects and affordability. Typically, patient access to penicillin allergy testing is limited by the availability of allergy specialists, who traditionally perform such testing. A pharmacist-provided penicillin allergy testing service was implemented at our hospital in 2015 and became a powerful antibiotic stewardship tool. Removing penicillin allergy from patient profiles significantly expanded therapeutic options, expedited discharges and reduced costs of care.

What is new: Pharmacists can expand patient access to penicillin allergy testing.

Conclusion: Pharmacist-provided penicillin allergy testing permitted optimized antibiotic treatment and expedited discharges.

KEYWORDS

antibiotic stewardship, pharmacist-run penicillin allergy testing, pharmacy clinical service

1 | WHAT IS KNOWN

According to the American Academy of Allergy, Asthma and Immunology (AAAAI), up to 10% of the US population reports a history of penicillin allergy.¹ However, most patients lose penicillin hypersensitivity over time due to the loss of IgE antibodies that mediate penicillin allergy.^{2,3} In fact, approximately only 10% of patients who report penicillin allergy are truly allergic.² Treatment options for patients who report penicillin allergy are significantly limited, leading to the use of broad-spectrum antibiotics that are often much more expensive or potentially less efficacious than penicillins. Such patients are prescribed broad-spectrum antimicrobials such as fluoroquinolones and vancomycin twice as often as patients without penicillin allergies.³ This practice contributes to increased antibiotic resistance,

higher costs of care and increased risks of adverse outcomes, such as *Clostridium difficile* infection or therapeutic failure.

The AAAAI recommends skin testing for all patients believed to be allergic to penicillin to verify this allergy.⁴

The Centers for Disease Control and Prevention has recommended that all patients reporting penicillin allergy should be evaluated and, if appropriate, tested for this allergy instead of being prescribed alternative broad-spectrum agents.⁵

Typically, patient access to penicillin allergy testing is limited by the availability of allergy specialists, who traditionally perform the great majority of allergy tests. Recently, other clinicians, particularly pharmacists, have begun to provide such testing, although few hospitals around the country offer pharmacist-provided allergy testing.⁶

Penicillin skin testing is the most reliable and safe method for assessing type I (IgE-mediated) reactions.^{2,3} Such reactions exhibit fast onset, typically within 1 hour after exposure, and involve the release of histamine by mast cells, which may cause urticarial rash, angioedema or anaphylaxis.⁷ The utility of skin testing is limited to type I (IgE-mediated) reactions. Other types of allergic reactions exist and should be excluded prior to testing. Type II (cytotoxic hypersensitivity) reactions are IgG- and IgM-mediated and involve antibodies reacting with antigens on the cell surface, leading to the activation of the complement system and thereby causing greater systemic effects. Manifestations of this hypersensitivity reaction can include haemolytic anaemia or thrombocytopenia upon exposure to particular antibodies.^{7,8} Type III hypersensitivity reactions arise from immune complexes that are deposited in tissues and prompt complement activation, which triggers an immune response. Clinical manifestations of such reactions include serum sickness, glomerulonephritis and vasculitis.^{7,8}

2 | OBJECTIVE

Our goal was to improve patient access to penicillin allergy testing by implementing a pharmacist-provided testing service in an inpatient setting.

3 | COMMENTS

Challenges facing pharmacists who wish to provide testing include a lack of standardized training programmes, a lack of experience providing such testing and limited experience with the implementation of such services in the hospital setting.

To improve patient access to pharmacist-provided penicillin allergy testing, we identified two specific aims:

1. To design a training programme for pharmacists.
2. To measure and examine the impact of penicillin allergy testing on antibiotic use by providers.

A training programme for pharmacists willing to provide penicillin allergy testing was developed by an infectious diseases pharmacist in collaboration with hospital physicians and utilized online video training materials offered by the manufacturer of the PrePen[®] benzylpenicilloyl polylysine injection (ALK-Abello, Inc., Round Rock, TX, USA). Any pharmacist employed by the hospital was eligible to be trained. The training programme consists of a didactic component and hands-on training. The didactic component of the training includes a review of mechanisms of drug hypersensitivity reactions, current AAAAI guidelines for allergy skin testing and the management of anaphylaxis, online videos regarding testing and instructions for appropriately reading and documenting test results. The hands-on training involves practicing the testing procedure on healthy volunteers. All newly trained pharmacists perform at least three consultations under the supervision of an infectious diseases pharmacist.

The Pharmacist-Provided Penicillin Allergy Testing Protocol detailing the testing procedure was developed in accordance with current AAAAI guidelines for allergy skin testing and based on input from hospital physicians and staff. The protocol was approved by the Pharmacy and Therapeutics Committee in May 2015.

Pharmacist-provided penicillin allergy testing is a consulting service that consists of four steps. Signed consent from patients is required for testing.

First step—Upon receiving a consultation request from a physician, an authorized pharmacist evaluates a patient's eligibility for testing. According to the protocol, patients are suitable for the test if they are at least 16 years old, not pregnant, not immunosuppressed, not on any medications that may interfere with the test and had an original allergic reaction that occurred more than 5 years ago and was consistent with an IgE-mediated response.²

Second step—If the patient is eligible, the pharmacist performs a skin scratch test utilizing normal saline (negative control), histamine solution (positive control), 10 000 units/mL of penicillin G (minor determinant) and PrePen[®] benzylpenicilloyl polylysine injection (ALK-Abello, Inc.). One drop of each solution is placed on a hairless area of the skin, typically the forearm or back; the skin is then scratched, and the patient is observed for 15 minutes.² A prick/puncture test result is considered positive if a wheal or flare reaction larger than that produced by the negative control (or a wheal larger than 3 mm) appears for either benzylpenicilloyl polylysine or dilute penicillin G.²

The purpose of utilizing benzylpenicilloyl polylysine and penicillin G is to ensure exposure to both major and minor determinants. The degradation products of penicillin can be divided into major and minor determinants. The major determinant, benzylpenicilloyl polylysine (PrePen[®]), is responsible for at least 80% of IgE-mediated penicillin reactions and is a commercially available product. Minor determinants are not currently commercially available; in this test, the minor determinant is compounded using penicillin G.^{3,6} The use of only the major determinant without a minor determinant can produce false-negative results for up to 10%-20% of patients who are truly allergic to penicillin. When both types of determinants are used, the negative predictive value of the skin test is close to 100%.²

Third step—Intradermal injections of the aforementioned solutions, with the exception of histamine, are administered, with tests read 15 minutes after intradermal injections. An intradermal test result is considered positive if a wheal or flare reaction larger than that observed for the negative control (or a wheal more than 3 mm larger than the original injection) appears for either benzylpenicilloyl polylysine or dilute penicillin G.²

Fourth step—patients with negative skin tests are given an oral challenge. Patients receive one dose of oral penicillin and are then observed for 60 minutes. This final step is particularly important because patients feel more confident taking beta-lactams in the future if they participate in this oral challenge under the supervision of a healthcare professional as part of a penicillin allergy test.

If a patient's test result is negative, penicillin allergy is removed from the patient's profile. A progress note detailing the patient's evaluation, testing procedure and results is written for every consultation.

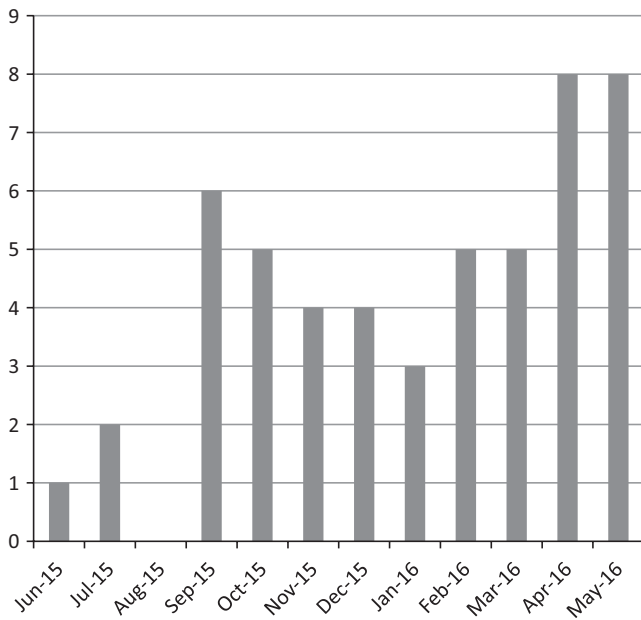


FIGURE 1 Number of penicillin allergy tests performed

Importantly, a positive skin test does not always mean that a patient is allergic to penicillin. The positive predictive value of the test is 40%-100%, given a prior history of allergy; the standard of care at our hospital is not to rechallenge patients who test positive on a penicillin skin test.²

Possible side effects of skin testing include rare local inflammatory responses at the testing site. According to AAAAI guidelines on allergy testing, the risk of systemic reactions from penicillin skin testing is extremely low and has mostly been associated with intradermal injections.² These guidelines emphasize the importance of prescreening with a prick/puncture test prior to intradermal injections to minimize risk.

From June 2015 through May 2016, our pharmacists tested 53 patients, and only two patients tested positive for penicillin allergy. The pharmacist-provided penicillin allergy testing service was well received by hospital providers. Physicians' confidence in the service and the popularity of the service among physicians have consistently increased over time. The number of tests performed increased from 3 per month to an average of 8 per month by the end of the 1-year period (Figure 1).

Most consultation requests were from internal medicine physicians, critical care physicians and infectious disease specialists. The use of the service continues to grow among specialists, especially surgeons and urologists (Figure 2).

The most common antibiotics used for the examined patients prior to testing were meropenem and vancomycin. After testing was performed and penicillin allergy was removed from the patient's profile, 40 of 51 patients (78%) who tested negative were switched to a narrower-spectrum beta-lactam. The most common beta-lactams utilized after testing were aminopenicillins. Nineteen of 51 patients (37%) were switched to oral beta-lactams and were discharged within 24 hours of testing, indicating that penicillin allergy testing

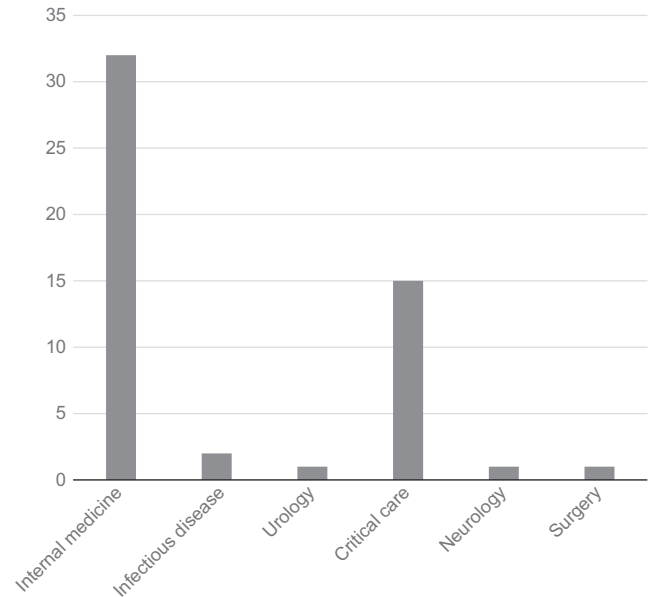


FIGURE 2 Consulting physicians

allows us to expedite discharges by expanding our choices of antibiotics. If it is assumed that the length of stay for those 19 patients was reduced by 1 day, then the estimated savings was ~\$30 000/year after subtracting costs associated with the penicillin allergy testing. Savings are estimated based on the average cost of a hospital bed per 24 hours.

4 | WHAT IS NEW

As one of the most easily accessible healthcare providers, pharmacists could potentially significantly expand patient access to penicillin allergy testing. This project describes a pharmacist-provided penicillin allergy testing service implemented at a community hospital. The service allowed for the optimization of antibiotic treatments and expedited discharges for many patients.

5 | CONCLUSION

Less than 0.1% of the 25 million individuals in the USA with a history of penicillin allergy undergo a penicillin skin test each year.⁹ Unfortunately, penicillin allergy testing is not routinely offered to patients in many healthcare settings, primarily due to a lack of providers trained to evaluate patients and perform such testing.

The existence of a pharmacist-provided allergy skin test can positively impact patient care by optimizing antibiotic regimens and accelerate discharges for patients while reducing healthcare costs.

Challenges facing pharmacists who wish to provide testing include a lack of standardized training programmes, a lack of experience providing such testing and limited experience with the implementation of such services in the hospital setting.

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